# Dissertation

## RECENT TRENDS IN LUNG CANCER

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requirement for

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# CERTIFICATE

This is to certify that this dissertation entiled **"RECENT TRENDS IN LUNG CANCER"** submitted by **Dr.R PRABHAKARAN,** appearing for part I and part II MD Tuberculosis and Respiratory Diseases degree examination in March 2007 is a bonafide record of work done by him under my guidance and supervision in partial fulfillment of regulations of The Tamil Nadu Dr.M.G.R.Medical University, Chennai. I forward this to The Tamil Nadu Dr.M.G.R.Medical University, Chennai, Tamil Nadu, India.

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# DECLARATION

I solemnly declare that the dissertation titled **"RECENT TRENDS IN LUNG CANCER"** is done by me at Institute of Thoracic Medicine and Govt. General Hospital, Chennai during 2005-2006 under the guidance and supervision of Prof.R.Atharunnisa Begum, M.D., D.T.C.D.

The dissertation is submitted to The Tamilnadu Dr.M.G.R.Medical University towards the partial fulfillment of requirements for the award of Degree in M.D. (Tuberculosis and Respiratory Diseases).

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# CONTENTS

# INTRODUCTION

Lung cancer is presently one of the most common malignancies through out the world. There has been an increase in incidence in the last 50 years. All histological types of lung cancer increasing incidence but different degrees. During a period of refinement of thoracic departmental lung cancer tumour registry it became apparent that along with an increasing incidence of lung cancer among women there was also an increasing prevalence of adenocarcinoma among lung cancer patients of both sex.

Primary studies in India show an increasing trend in lung cancer compared to a quarter of century ago. Studies from India have emphasized significant epidemiological and cell type difference that exist in the country compared to that reported in the west. The increase in incidence of bronchogenic carcinoma is not only due to better diagnostic facilities like flexible fibreoptic bronchoscopy but also other factors like increase in number of smokers, increasing environmental pollution and increase in number of people living in higher age groups.

# AIM OF STUDY

An open prospective study was undertaken to study the recent profile of Lung cancer.

# REVIEW OF LITERATURE

## A. EPIDEMIOLOGY

### Age

Bronchogenic carcinoma is mainly a disease of middle age. However it may develop in very old and in children. It has been recorded in a child as young as 10 years. The peak frequency of bronchogenic carcinoma is between 50 to 60 years in India and the incidence below 40 years is less frequent. The average age of brochogenic carcinoma was 51.7 years in a study conducted by Jindal.

### Sex

Bronchogenic carcinoma is predominantly a disease of men. But the incidence is steadily increasing in females in most industrialized countries. The male female ratio was 4.1:1 in conducted by Jindal and Behera in 1990.

## Smoking

The suspicion that smoking could cause cancer was first noticed in 1761 when John Hill reported the occurrence of polyps in snuff takers. Ochsner in 1971, first recognised the relation between smoking and increasing incidence of lung cancer.

In a study conducted by Jindal and Behera in India, the overall smoker: non smoker ratio was 2.68:1. The study was conducted over 1009 patients over 10 years. Different studies overall the world have established the following observations.

1. Cigarette smokers are ten times likely to develop lung cancer in comparison to life long non smokers. The extent of risk correlates with the number and duration of cigarette smoked and risk of lung cancer decreases as the period of abstinence increases.

    a. Filter cigarette are less harmful. Beedi smoking which is a common practice in India is equally if not more harmful than cigarette.

2. The principal carcinogenic agent is the inhaled combustion product of the particular matter (tar). Particular attention has been paid to

aryl hydrocarbon hydroxylase (AHH) which converts polycyclic hydrocarbons found in cigarette smoke to metabolites that are potent cacinogens.

3. Passive smoking (air pollution from another person's tobacco smoke) plays a prime role in causation of lung cancer (Svendsen et al.,)

4. Risks of cigarette smokers are much lower in our country as compared to the western countries.

## Occupational factors

Information about occupational carcinogenesis is adequate due to lack of large number of epidemiological study and the long lag period between the exposure and clinical manifestation. Smith et al., found average benzo(a)pyrene exposure during cooking period from 4 villages in western India to be nearly 4000 ng/m3 and it is equivalent to smoking 20 cigarette per day. Asbestos fiber increases the incidence of lung cancer and cigarette smoking greatly increases (90 fold) the incidence of lung cancer in asbestos workers. Inhalation of decay products of radon is the predominant carcinogenic influence i.e. more than that of radon itself.

Other agents line arsenic, nickel, chromium, chloroethylether, mustard gas are associated with increased incidence of lung cancer.

## B. HISTOLOGICAL CLASSIFICATION OF LUNG CANCER

Considering the heterogeneity of lung cancer, WHO has provided an appropriate basic nomenclature of lung cancer based on light microscopy (1981)

1) Squamous cell carcinoma

   Variants: spindle cell (squamous)carcinoma.

2) small cell carcinoma

   a) Oat cell carcinoma

   b) Intermediate cell type

   c) Combined oat cell carcinoma

Adenocarcinoma

   d) Acinar

   e) Papillary

   f) Broncho-alveolar carcinoma

   g) Solid carcinoma with mucous production

3) large cell carcinoma

    a) Gaint cell carcinoma

    b) Clear cell carcinoma

4) Adenosquamous carcinoma

5) Carcinoid tumors

6) Bronchial gland carcinoma

    a) Adenoid cyst carcinoma

    b) Muco- epidermoid carcinoma

    c) others.

7) Others

## Recent classification of Invasive Malignant Tumor by WHO

1999, 3rd Berlin, Germany: Springer-Verlag.

1. squamous cell carcinoma

    Variants

        Papillary

        Clear cell

        Small cell

        Basaloid

2. small cell carcinoma

    Variants

        Combined small cell carcinoma

3. Adenocarcinoma

    Acinar

    Papillary

    Bronchiolalveolar carcinoma

        Non Mucinous (Clara cell/type2 Pneumocyte)

Mucinous (goblet cell type)

Mixed mucinous and non mucinous

(Clara cell/type 11 pneumocyte and goblet cell type) or indeterminate.

Solid Adenocarcinoma with mucin formation

Mixed

## Variants

Well differentiated fetal Adenocarcinoma

Mucinous (colloid)

Mucinous cystadenocarcinoma

Signet ring

Clear cell

4. Large cell carcinoma

Large cell neuroendocrine carcinoma

Basaloid carcinoma

Lymphoepithelio like carcinoma

Clear cell carcinoma

Large cell carcinoma

Large cell carcinoma with rhabdoid phenotype

5. Adeno squamous carcinoma

6. Carcinomas with pleomorphic, sarcomatoid or sarcomatous elements.

Carcinoma with spindle and/or gaint cells.

Pleomorphic carcinoma

Spindle cell carcinoma

Giant cell carcinoma

Carcinosarcoma

Blastoma (pulmonary blastoma)

Others

## C. CLINICIAL MANIFESTATIONS

Bronchogenic carcinoma presents with diverse clinical manifestations. Clinical features may be due to the following reasons:-

### 1. CLINICAL FEATURES DUE TO PRIMARY TUMOUR

Centrally located tumours produce different symptoms than do peripherally located tumours.

#### Clinical features due to central tumours

#### Cough

It is the commonest symptom and occurs in i75% or more patients. Cough may be produced by a Small tumour acting as a foreign body interfering with bronchial peristalsis or by neoplastic erosion of bronchial mucosa.

#### Chest pain

It is vague , persistent and poorly localized.It is due to peribronchial and perivascular nerve involvement.

## Dysponea

It occurs in approximately 58%of patients. It may be due to Emphysema, pleural effusion,atelectasis, bronchopulmonary Infection, phrenic nerve paralysis and O2 transport defect in broncho-aveolar carcinoma

## Hemoptysis

It occurs in 5 to 51% of patients . it is usually scanty and is due to ulceration of bronchial mucosa

## Wheeze

It occurs in 2% cases. It is due to fixed mechanical obstruction below the carina & it is not changed after cough.

## Stridor

It is due to narrowing of trachea & main bronchi at the level of carina.

### Fever and sepsis

It is due to post obstructive pneumonia.

## 2.CLINICAL FEATURES DUE TO PERIPHERAL TUMOURS

### Pleuritic chest Pain

It is either due to involvement of the parietal pleura or due to pleurisy arising as a result of post obstructive segmental or sub segmental pneumonia.

### Dyspnoea

It is restrictive in nature. It is either due to pleural effusion or due to pleuritic chest pain.

### Cough

It is less common except in broncho-alveolar carcinoma.

## Clinical features due to intrathoracic spread

### Neurological complications

Due to involvement of 8th cervical and 1st thoracic nerve the patient will present with characteristic pain in the shoulder and in the arm along the distribution of ulner nerve. Sensory loss with weakness and wasting of small muscles of the hand will occur. Patient may present with horner syndrome due to involvement of cervical sympathetic nerve. Involvement of recurrent laryngeal nerve produces hoarseness of voice & dysphagia (common on the left side). Diaphragmatic palsy due to phrenic nerve damage is a possibility. Erosion of ribs (commonly 1st and 2nd) may occur.

### S.V.C Obstruction

It is obstructed either by primary tumours or by metastatic lymph nodes. It was first described by William Hunter in 1757. Obstruction may be above or below the azygos vein. The common presenting symptoms are oedema of the head, neck, arms, breasts, dyspnoea, cough, and orthopnoea. The oedema is pitting and varies with changes in position. Collateral veins fill from above downwards. Its incidence ranges from 4 to 19%.

### Pleural and pericardial effusion

Pleural effusion is commonly due to direct involvement of pleura by tumour. It may be due to lymphatic obstruction or disruption of thoracic duct (chylothorax). Features of cardiac tamponade, sinustachycardia or atrial fibrillation may appear due to involvement of pericardium or heart.

### Dysphagia

It may occur due to compression of oesophagus by posterior mediastinal gland. Immediate cough upon swallowing may occur due to broncho-pleural fistula.

Pulmonary artery constriction or pulmonary artery stenosis (extrinsic) may occur due to tumour involvement.

## 3. CLINICAL FEATURES DUE TO EXTRATHORACIC METASTASIS

Extrathoracic metastasis is common in small cell carcinoma. It may involve any organ or tissue, but lymphnode, brain, liver, adrenal and skin

are commonly involved. Bone and brain involvement usually produce symptoms and others are usually silent

## Central nervous system

Metastasis may involve the brain, meninges and spinal cord. Spinal cord involvement produces back pain which is localized and progressive in nature. Other symptoms are numbness, tingling, weakness, of an extremity, bladder and bowel disturbance and unsteadiness of gait. Due to intracranial involvement patient may present with headache, vomiting, altered mental status, weakness, seizures, cranial nerve abnormality, hemiparesis and cerebellar ataxia**.**

## Lymph node metastasis

Lymphatic spread is common in small cell carcinoma, the whole of right lung and lower lobe of left lung ultimately drains into right suparclavicular gland via hilar and paratracheal nodes. Upper lobe of left lung drains into the para aortic, hilar and carnial nodes. Enlarged gland is usually painful and hard in consistency.

### Bone metastasis

It produces distressing and unremitting pain which may be due to pathological fracture or bone erosion.

### Hepatic metastasis

Enlarged palpable liver and unusual. Hard and irregular liver suggests hepatic metastasis.

### Skin metastasis

It may occur occasionally.

### 4. Paraneoplastic syndrome

Paraneoplastic syndromes are non-metabolic or neuromascular complications of lung cancer. It occurs in small cell carcinoma. Ectopic hormones are produced from the neurosecretory granules within the malignant cells.

# METABOLIC DISORDERS

## Hypercalcemia

It is caused by ectopic parathormone secretion by tumour cells. It commonly occurs in squamous cell carcinoma. It is seen in about 10% of cancer patients. Patients present with thirst, polyuria nocturia, nausea, vomoiting, anorexia, abdominal pain, mental confusion, hypotonia, stupor and ultimately coma.

## Syndrome of inappropriate antiduresis

It is commonest of the syndrome of tumour hormonogenesis (2-22%) and common in small cell carcinoma. Patients present with headache, drowiness, mental confusion, disorientation, convulsion, coma, hypothermia and death.

## Clinical syndrome due to excess ACTH

It is fairly uncommon (2%) and is widely variable in severity.patients present with dependent oedema, pigmentation, weakness and wasting muscles particularly of limb gridle. Hypertension and hyperglycemia may be present. Cushing’s syndrome is unusual.

### Clinical syndrome due to other hormone

Oxytocin, GHRH,somotostatin, neurophysin, lipotrophin, prolactin, calcitonin gastrin, glucogon etc may be produced by tomour cells. Very rarely these hormones produce symptoms

## NEUROLOGIC AND NEUROMASCULAR DISORDER

### Peripheral neuropathy

Commonly seen in small cell carcinoma. It may be motor, sensory or mixed and may be accompanied by muscle wasting or weakness.

### Autonomic neuropathy

It may produce postural hypotension and intestinal motility. Cerebellar ataxia with nystagmus, impaired co-ordination and dysarthria may occur.

### Polymyositis/ dermatomyositis syndrome

It is characterized by proximal muscle weakness, pain and tenderness and a characterized facial heliotrope rash.

## Myasthenic syndrome

Patients present with muscle weakness and in contrast to myasthenia gravis it improves with repeated effort. Other differentiating points are muscular wasting, loss of tendon reflex and infrequency of bulbar involvement.

## Hypertrophic pulmonary osteoarthropathy

It was first described by Bomberger (1889) and Marie (1890). Thompson (1904) first described its association with lung cancer. It's incidence varties from 2 to 48%. Patients present with bone pain in the involved areas which are often hot and tender to touch. There may be associated pain and swelling of the wrists, ankles and knee joints. Clubbing occurs in 90% of cases. It is commonly associated with adenocarcinoma.

## Gynaecomastia

It may occur occasionally. The histological types most frequently found are large cell and adenocarcinoma. Clinical features related to other systems are given below in the tabulated form.

## Dermatologic

Pigmentation, pruritus, lanugohirsuitism ,acanthosis nigricans and erythema gyratum nigricans.

## 8. Vascular

Thrombophlebitis migrans, arterial thrombosis and non bacterial thrombotic endocarditis.

## Hematologic

Anaemia, hemolytic anaemia, red cell aplasia, thrombocytopenic purpura, intravascular coagulation, hypofibrinogenemia and eosinophilia.

## Immunologic

Dermatomyositis, systemic sclerosis, membranous glomerulo nephritis & rickets.

## General systemic

Pyrexia, anorexia, cachexia and taste dysfunction.

## D.INVESTIGATIONS

### 1. Conventional chest radiography

Radiological manifestation differs in centrally located and peripherally located tumours. Slight prominence of hilar shadow is the early radiologic finding of centrally located tumours. Peripherally located tumours initially present as a small nodule. Squamous cell carcinoma is centrally located in 65%of cases. It may persent as ill defined hilar mass which represents a summation of primary mass, consolidated lung & metastatic adenopathy. Due to partial or complete obstruction of bronchus it may present as post obstructive preumonitis or collapse. Collapse may be segmental, lobar or whole lung. Diaphragm is elevated if phrenic nerve is involved. Peripheral nodules are often very large, the borders of the nodule are often poorly defined or lobulated. The mass of squamous cell carcinoma frequently cavitates due to cetral necrosis. The cavities are typically thick walled with an ir regular inner surface, squamous cell carcinoma is the frequent cause of pancoast tumour. Adenocarcinomas present as peripheral mass in 60 to 70% cases. The peripheral nodules is usually round or oval in shape. They are ill defined or lobulated or sunburst appearance. It may present as a slow growing or fairly stable peripheral nodules. Adenocarcinoma may present as central; mass.

Broncho-alveolar carcinoma most commonly present as a very slowly growing circumscribed localized nodule. One unique feature of this nodule is the presence of air bronchogram. The diffuse forms of alveolar cell carcinoma includes an ill defined mass, coalescent multinodular infilterate and lobar consolidation. Other radiographic manifestation are pleural effusion (8- 10%) atelectasis, pneumothorax or cavitation.

Large cell carcinoma presents like adenocarcinoma. It is frequently larger than 4 cms in diameter. Poorly defined or lobulated margin is common. Small cell carcinoma is usually small and it is difficult to detect on a radiograph. Radiologically most typically it is manifested as a central mass due to involvement of ipsilateral hilar or madiastinal lymphnodes. It is the least common cause of peripheral mass

## Unusual radiographic manifestations

a) Spontaneous regression or decrease in size

b) Calcification

c) Thin walled cavity

d) Meniscus or air crescent sign

e) Alveolar pattern

f) Satellite nodules

g) Double lesion sign

h) Mucoid impaction

i) Obstructive hyperinflation

j) Spontaneous pneumothorax

k) Diffusion nodular pleural tumour spread

l) Loculated pleural effusion

## 2. Sputum cytology

Examination of 5 separate sputum sample using the papanicolaou staning of fixed sputum smear can detect 70-80% of all primary tumours. The yield is better for centrally located tumours (80%) than for peripherally located tumours (42%). The more productive times to collect specimens are in the immediate post bronchoscopy period or when the patient is raising blood streaked sputum. The following are the factors influencing the ratr of detection of malignant cells in sputum.

a) Large tumour size

b) central tumour location

c) Exfoliating carcinoma

d) lack of tumour differentiation

e) Histological type

f) Lobe of the lung involved.

The first sputum of the morning is usually product of deep cough and tends to produce a higher positive yield. Induced sputum is more representative. Sputum may be collected by transtracheal aspiration, tracheobronchial aspiration or bronchoscopic aspiration. Early diagnosis is possible by cytology but prognosis does not change.

### 3. Fine needle aspiration cytology (percutaeneous)

The cytodiagnosis of lung nodules has improved during the last decade due to improved localization technique (CT scan and ultrasound). Lesions less than 1 cm in diameter can be successfully aspirated using 21 to 23 gauge needles. The presence of new or peripheral localized lung lesion less than 2 cm in diameter, located in the outer 1/3$^{rd}$ of the lung and not visualized through bronchoscope constitutes an indication for FNAC.

## 4. Bronchoscopy

Killian first introduced rigid bronchoscope in 1897. Ikeda's introduction of the flexible fibreoptic bronchoscope in 1966 has made a great impact on the practice of respiratory medicine. A major advance has been achieved in visualizing, and sampling, bronchial pathology very much more peripherally than rigid bronchoscope. It can be introduced with local asaesthesia and complication is remarkably low. Among patients with central or hilar masses, bronchoscopy is diagnostic in 68 to 98% cases. For peripheral nodular or masses it is diagnostic in approximately 50%cases. Abnormalities in the lung apices and superior basal segments of lower lobes may be difficult to approach by fibreoptic bronchoscope. Bronchoscopically, tumours, or metastatic hymph node enlargements may produce visible changes of three main types:

1. Simple distortion of the normal anatomy by external pressure on bronchial tree
2. involvement of the bronchial wall with local distortion or ulceration of the mucosa and
3. intraluminal eruption of the growth.

Obtaining specimens from the bronchial tree during endoscopy is a vital part of diagnosis of bronchogenic carcinoma. Material may be produced by the following methods:

### a. Aspiration of bronchial secretion

With a specimen trap in circuit, gross specimen of secretion can be obtained directly via the aspirating channel of the fiberscope. Maximum yield is obtained by drawing a little normal saline through the instrument at the end of the operation. Diagnostic yield is high when the mass is endobronchial and centrally located, particularly situated in lower lobes.

### b. Bronchial brushing

Brusing taken from the surface of area suggesting tumour tissue frequently give positive diagnoses. The method is particularly useful in small bronchi, where the forceps will not open or when used blindly where a tumour beyond vision is suspected.

### c. Endobronchial biopsy

The most critical bronchoscopic manoeuvre is taking the biopsy. The specimen obtained is very small but usually adequate because it’s

source can be clearly chosen. All specimens are placed in 10% formol-saline for transport to the laboratory. Haemorrhage has to be avoided.

### d. Transbronchial needle aspiration

Sometimes the best chancve of reaching a diagnosis bronchoscopically, when no intraluminal lesion is found, is to obtain biopsies from enlarged lymph nodes that are obviously distorting bronchi. Transbronchial needle aspiration is the safest technique here. Strong aspiration through a wide bore needle will remove tissue for cytological examination.

### e. Transbronchial lung biopsy

It provides one of the safest ways of obtaining small biopsies of the lung parenchyma particularly when the disease is diffuse.

### f. Biopsy of peripheral lesions

The procedure is undertaken in radiographic department under fluoroscopic guidance. Radiologically controlled, percutaneous needle biopsy of small peripheral lesions is quicker and more accurate.

## 5. Computed tomography and MRI

In patients with tumour of bronchial orgin, CT scanning provides detailed information critical to accurate tumour staging. CT scanning has provided especially valuable as a complementary procedure to fibreoptic bronchoscopy. As compared with CT, at present the role of MR imaging is less well defined. Preliminary data suggest that in the diagnosis of mediastinal adenopathy it provides similar results to those obtained with CT.

## 6. Investigations for secondary metastasis

For lumph node metatasis fine needle aspiration cytology and biopsy of the suspected node mey be done. To exclude hepatic metastasis liver function tests,isotope scan, ultrasound investigation frequently misses metastssis. Biopsy under direct vision is the best for positive histology.

For suspected brain metatasis the confirmatory investigation of choice is computed tomography with contract enhancement. Cytological examination of C.S.F may be done in suspected case of meningeal involvement.

Barium swollen x-ray or CT scan is done to exclude esophageal compression by metastasis lymphnodes. Fluoroscopy may be done to exclude diaphragmatic palsy. For suspected bone involvement ,elevated levels of alkaline phosphatase and gamma gultamyl tranferase may be helpful. Bone scanning is much more sensitive than conventional x-ray and false negative result is less than 2%.

Cytological examination of pleural fluid for malignant cells may be helpful for diagnosis.

## 7. Bio-chemical and hormonal changes

In tumour associated ACTH secretion, the measurement of ACTH and its associated peptides in blood is of limited value because of significant false positive and false negative results. Usually plasma cortisol conc.exceeds 30 g/dl and plasma corticotrophin is persistently high, above 200 g/ml. urinary excretion of unbound cortisol and cortisol metabolites is abnormally high. Plasma k+ is less than 3.3 meq/L with high plasma bicarbonate and alkaline pH. Glucose intolerance is sometimes present.

Periodic assessment of serum calcium is obligatory in the management of lung cancer. Bronchogenic carcinoma associated

parathormone is not similar to conventional parathormone. So parathromone estimation is of limited value. These patients may differ from those of primary hyperparathyroidism in tht they intend to be more severely hypercalcemic (serum conc > 14mg/dl)

Cancer should always be included in the different diagnosis of patients who present with hyponatremia. It is due to inappropriate secretion of ADH by tumour cells. ADH measurement by radio-immunoassay has demonstrated that more than 30% of small cell carcinoma patients has a high concentration ofADH in blood. Sodium concentration becomes low. Plasma osmolality becomes less than 260 mosmo/kg H2O (normal 285-295 mosmo/KgH2O) and urine osmolality rises (usually 400-500 mosmo/KgH2O).

# MATERIALS AND METHODS

An open prospective study of patients who attended THORACIC Medicine Department at Government General Hospital Chennai, and Institute of Throracic Medicine, Chetpet, with clinical and/or radiological suspicion of lung cancer was studied over a period of 12 months between January 2005 and 2006. The study protocol included a detailed history regarding the onset and progress of the disease, smoking habits and other associated risk factors if any.

Inclusion criteria

All the patients who had clinical features and radiological abnormalities suggestive of lung cancer have been included.

Exclusion criteria:

Among the patients included in this study those did not have histopathological proof have been excluded and the remaining were analysed.

The complaints which were evaluated in detail included cough, sputum, chest pain, dyspnea, fever, weight loss, hoarseness of voice, dysphagia and symptoms suggestive of SVC obsturuction, paraneoplastic

syndromes and systematic metastasis. A detailed general and systematic examination was preformed. All patients were subjected to baseline blood investigations, chest x ray PA and lateral view, ultrasound abdomen and chest. Computerized Tomography of chest was done to characterize the lesion further and t help to arrive at tissue diagnosis. FOB was done in some patients to detect and aid in getting at histopathological diagnosis.

Following investigations helped in the histopathological confirmation of the diagnosis.

1. Computerized Tomography guided needle biopsy

2. Ultrasound guided needle biopsy

3. Endobronchial biopsy with Fiberoptic bronchoscopy

4. Excision biopsy of supraclavicular node

5. Pleural fluid cytology.

Fiberoptic bronchoscope was performed with a single channel (pentax, Japan).Bronchoscope (pentax,Japan). Under local anesthesia, 2ml of 2% Lignocaine was injected transtracheally after test dose along with spraying of 4% lignocaine using hand atomizer just prior to the

procedure. Lignocaine jelly was applied to the effective length of Fiberoptic bronchoscope. The Fiberoptic bronchoscope was passed transnasally in the supine position. The normal side was visualized first and then the suspected abnormal side. Biopsy was performed in patients with obvious endobronchial lesion. Mucosal brushings were-obtained from the area surrounding the abnormal segment on radiological basis in case of patients without endobronchial lesion. A central tumour was defined as a tumour that was evident within the ebronchial tree at Fiberoptic bronchoscopy and a peripheral tumor as one that was not visualized at bronchoscopy. Xray wise central tumor was defined as tumors arising beyond the hilum. A post bronchoscopic sputum was sent. Patients were subjected to percutaneous lymphnode aspiration and cytology.

Computerized Tomography/Ultrasound guided needle biopsy was done in patients when indicated. The biopsy was done using Atovac gun, core biopsy needle. The needle size was 8G, 10cm to 15cm in length with 1cm markings. The distal tip was ultrasound sensitive, the needle also has an over sheath cannula for computerized Tomography guidance. The needle length was adjusted using pins. With computerized Tomography/Ultrasound guidance the lesion was localized, under cover

of local anesthesia the needle length was adjusted according to the lesion and core biopsy obtained which was 2cm to 3cm bit. In indicated patients pleural fluid aspiration cytology was done under aseptic precaution with adequate local anesthesia.

The specimens obtained were:

Computerized Tomography guided needle biopsy

Fiberoptic bronchoscope brushing and biopsy

Ultra sound guided- Needle biopsy.

Smears for cytology were fixed in isopropyl alcohol for 30mts and stained with Hematoxylin and eosin stain. Smear was air dried and fixed in methanol for 30 minutes. All dried smears were fixed with MGG (may grunwald Giemsa) stain, slides were mounted and reported under microscope by cytopathologist.

Biopsy specimens were fixed in formaldehyde (10%) for 24 hrs and auto processed. These slides were stained with hematoxylin and eosin and reported by pathologist. Special stains were used as required. Pleural fluid was centrifuged and smears stained in Hematoxylin and eosin.

# RESULTS

123 Patients were included in the study. Pathological diagnosis was possible in patients. Eleven patients in whom cell type diagnosis was not possible the procedure done for pathological diagnosis were inconclusive. The eleven patients had x-ray features suggestive of mass lesion along with computerized tomography of the chest confirming the same. In these eleven patients malignant cells could be identified but the exact cell type diagnosis was not possible.

Age: In our study the age ranges from 28-82 years.

## AGE INCIDENCE IN THIS STUDY

| Age in years | No. of patients | Percentage |
|---|---|---|
| <39 | 6 | 4.87 |
| 40-49 | 22 | 17.88 |
| 50-59 | 33 | 26.82 |
| 60-69 | 45 | 36.58 |
| >70 | 17 | 13.82 |
| Total | 123 | 100.00 |

Sex: No. of Males : 107

No. of Female : 16

Male, Female ratio was 6.6:1

## SEX INCIDENCE OF LUNG CANCER IN RELATION TO CELL TYPES IN THIS STUDY

| Type | Female | | Male | |
|---|---|---|---|---|
| | No | % | No | % |
| Squamous cell carcinoma | 2 | 1.78 | 62 | 55.35 |
| Adenocarcinoma | 12 | 10.71 | 29 | 25.89 |
| Small cell carcinoma | nil | nil | 4 | 3.57 |
| Large cell carcinoma | nil | nil | 2 | 1.78 |
| Mucoepidermoid carcinoma | nil | nil | 1 | 0.892 |
| Total | 14 | 12.49 | 98 | 87.51 |

## Clinical features

The pulmonary symptoms most commonly presented were cough was present in103 patients (83.79%) followed by chest pain in 65 patients (52.84%) and dyspnea in 71 patients (57.72%), hemoptysis in 39 patients (31.70%), 24 patients (19.51%) of the 123 patients included in this study gave history suggestive of treatment for tuberculosis in the past and most common cell type associated was adenocarcinoma.

## HISTOLOGICAL TYPES AND SYMPTOMATOLOGY

| Symptom | Cell type | | | | | | | | | | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Squamous carcinoma | | Adeno carcinoma | | Small cell carcinoma | | Large cell Carcinoma | | Mucoepidermoid Carcinoma | | |
| | no | % | no | % | No | % | no | % | No | % | |
| Cough | 63 | 61.63 | 30 | 29.12 | 3 | 2.91 | 2 | 1.94 | 1 | 0.97 | 103 |
| Dyspnea | 55 | 77.46 | 14 | 19.71 | 1 | 1.4 | 1.4 | 1.4 | Nil | nil | 71 |
| Chest pain | 49 | 75.38 | 12 | 18.46 | 3 | 4.61 | 1 | 1.53 | Nil | nil | 65 |
| Hemoptysis | 30 | 76.92 | 5 | 12.82 | 3 | 5.08 | 1 | 2.56 | nil | Nil | 39 |

## Smoking

97 patients were smokers, 26 patients were non smokers. None of the females in this study were smokers.

### SMOKING INDEX AND NUMBER OF PATIENTS

| Smoking index | Patients | Percentage |
|---|---|---|
| 0 | 26 | 21.38 |
| <100 | 2 | 1.62 |
| 100-300 | 16 | 13.00 |
| >300 | 79 | 64.22 |
| Total | 123 | 100.00 |

The most common cell types among smokers were squamous cell carcinoma. 26 patients were non smokers. Among non smoking patients the most common pathological diagnosis was adeno carcinoma14 (53.84%), followed by squamous cell carcinoma 9 patients (34.61%).

## HISTOPATHOLOGICAL TYPES RELATED TO SMOKING

| Feature | Squamous cell carcinoma | | Adeno carcinoma | | Small cell carcinoma | | Large cell carcinoma | | Muco epidermoid | | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | **No** | **%** | **No** | **%** | **No** | **%** | **No** | **%** | **No** | **%** | |
| Smoking | 55 | 63.95 | 24 | 27.9 | 4 | 4.65 | 2 | 2.32 | 1 | 1.62 | 86* |

* Typed patients only included

### Passive smoking

2 female patients gave definite history suggestive of passive smoking. One male had the history of passive smoking.2 had adenocarcinoma and patients had squamous cell carcinoma.

## Clubbing

41 (33.33%) patients presented with clubbing. All patients with small cell carcinoma had no clubbing.

### TYPES OF LUNG CANER AND CLUBBING

| Type | Patients | % |
|---|---|---|
| Squamous cell Carcinoma | 27 | 65.85 |
| Adeno carcinoma | 12 | 29.26 |
| Small cell carcinoma | Nil | Nil |
| Large cell carcinoma | 1 | 2.4 |
| Mucoepidermoid | 1 | 2.4 |
| Total | 41 | 100 |

## Chest X-ray features

The most common presentation was mass lesion

## RADIALOGICAL FEATURES OF DIFFERENT CELL TYPES

| Type of Lesion | Squamous Cell | | Adeno carcinoma | | Small cell carcinoma | | Large cell carcinoma | | Muco epidermoid | | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | No | % | No | % | No | % | No | % | No | % | |
| Right side | 34 | 50.74 | 27 | 40.29 | 3 | 4.47 | 2 | 2.98 | 1 | 1.49 | 67 |
| Left side | 30 | 63.82 | 16 | 34.04 | 1 | 2.12 | Nil | Nil | Nil | Nil | 47 |
| Hilar mass | 10 | 47.61 | 8 | 38.09 | 2 | 9.52 | Nil | Nil | 1 | 4.76 | 21 |
| Pulmonary mass | 45 | 71.42 | 15 | 23.8 | 1 | 1.58 | 2 | 3.17 | Nil | Nil | 63 |
| Cavitary mass | 2 | 100 | Nil | Nil | Nil | Nil | Nil | Nil | Nil | Nil | 2 |
| Mediastinal Widening | 6 | 85.71 | Nil | Nil | L1 | 14.28 | Nil | Nil | Nil | Nil | 7 |
| Consolidation | 3 | 60 | 2 | 40 | Nil | Nil | Nil | Nil | Nil | Nil | 5 |
| Collapse | 10 | 100 | | | Nil | Nil | Nil | Nil | Nil | Nil | 10 |
| Coin lesion | | | 3 | 100 | Nil | Nil | Nil | Nil | Nil | Nil | 3 |
| Rib erosion | 6 | 100 | | | Nil | Nil | Nil | Nil | Nil | Nil | 6 |
| Pleural Effusion | 16 | 47.05 | 18 | 52.95 | Nil | Nil | Nil | Nil | Nil | Nil | 34 |
| Pericardial effusion | 2 | 100 | Nil | Nil | Nil | Nil | Nil | Nil | Nil | Nil | 2 |
| Diaphragm elevation | 2 | 100 | Nil | Nil | Nil | Nil | Nil | Nil | Nil | Nil | 2 |

Sputum cytology was positive in 6 patients (4.87%) and most common tumor associated was squamous cell carcinoma. Post bronchoscopic sputum cytology was positive in 8 patients (6.5%) and most common cell associated was squamous cell carcinoma.

SVC obstruction was seen in 8 patients (6.50%) and most common cell type was squamous cell carcinoma 5 patients (62.5%), small cell 2 patients ( 25 %), CNS metastasis was seen in 9 patients (7.31%) and most common cell type was adenocarcinoma 6 patients (71.428%), liver metastasis was present in 2 patients (1.62%) and most common cell type was squamous cell carcinoma. Hoarseness of voice was present in 9 patients (7.31%) and actual vocal cord palpsy was present in 7 patients.

Computerized Tomography scan was done in 98 patients. Computerized Tomography helped in histopathological diagnosis by way of computerized Tomography guided needle biopsy of suspected mass in 60 patients, positive results was obtained in 45 (75%). The pathological diagnosis could not be got through computerized Tomography guided biopsy in 15 patients. Positive brochus sign was present with rib/ vertebral metastasis, 9 patients with mediastinal modes, 2 patients with nodules in the lung, 2 patients with rib erosion, 1 patient with military

carcinomatosis, 1 patient with malignant effusion and pleural nodules, all which were not seen on chest x-ray.

Fiberoptic bronchoscope was done in 56 patients. 80%had cenetral tumors. Bronchial cytology yielded positive results in 31 (55.39%). Endobronchial biopsy yielded positive results in 11 (73.33%) of the 15 performed patients.

Supracalvicular node biopsy yielded positive results in 12 patients.pleural fluid cytology was positive for malignant cells in 14 patients.

The interventional procedures had very minimal complications with no mortality. 3 patients developed pneumothorax during computerized Tomography guided biopsy, of which only 1 patient needed intercostals drainage, the rest settled with symptomatic treatment, 2 patients had minimal hemoptysis. During fiberoptic bronchoscope 5 patients had hemoptysis which was mild to moderate.

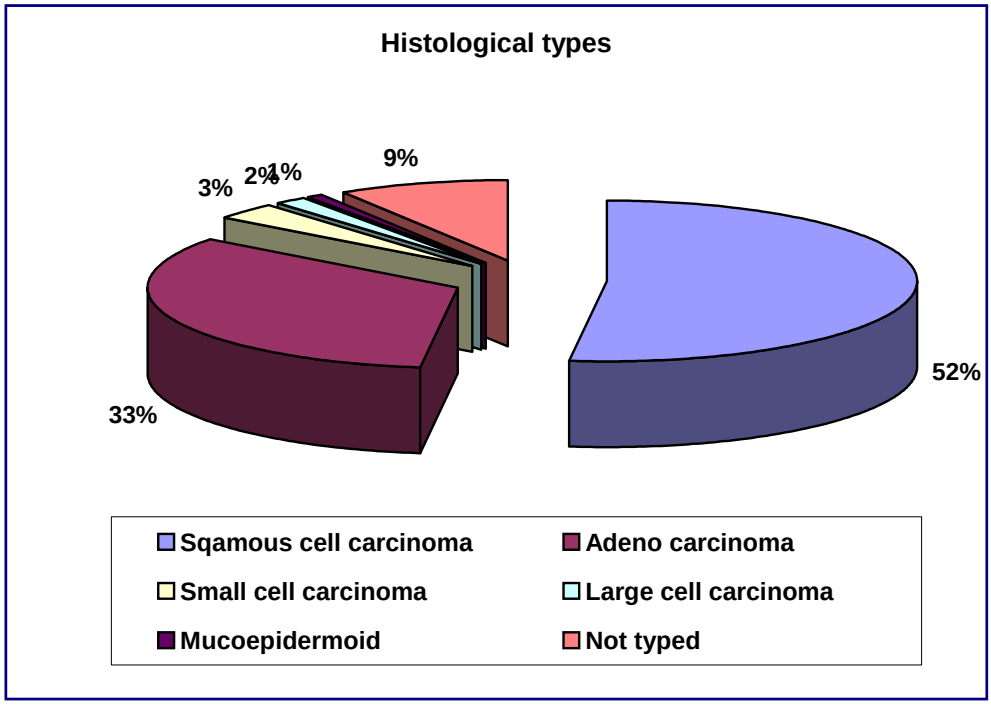
## MODALITIES USED TO PROVE CARCINOMA

| Modality | Number | percentage |
|---|---|---|
| Fiberoptic bronchoscope | 42 | 34.14 |
| Ultrasonogram | 29 | 23.57 |
| Computerised tomogram | 26 | 21.13 |
| Node biopsy | 12 | 9.75 |
| Pleural fluid cytology | 14 | 11.38 |
| Total | 123 | 100.00 |

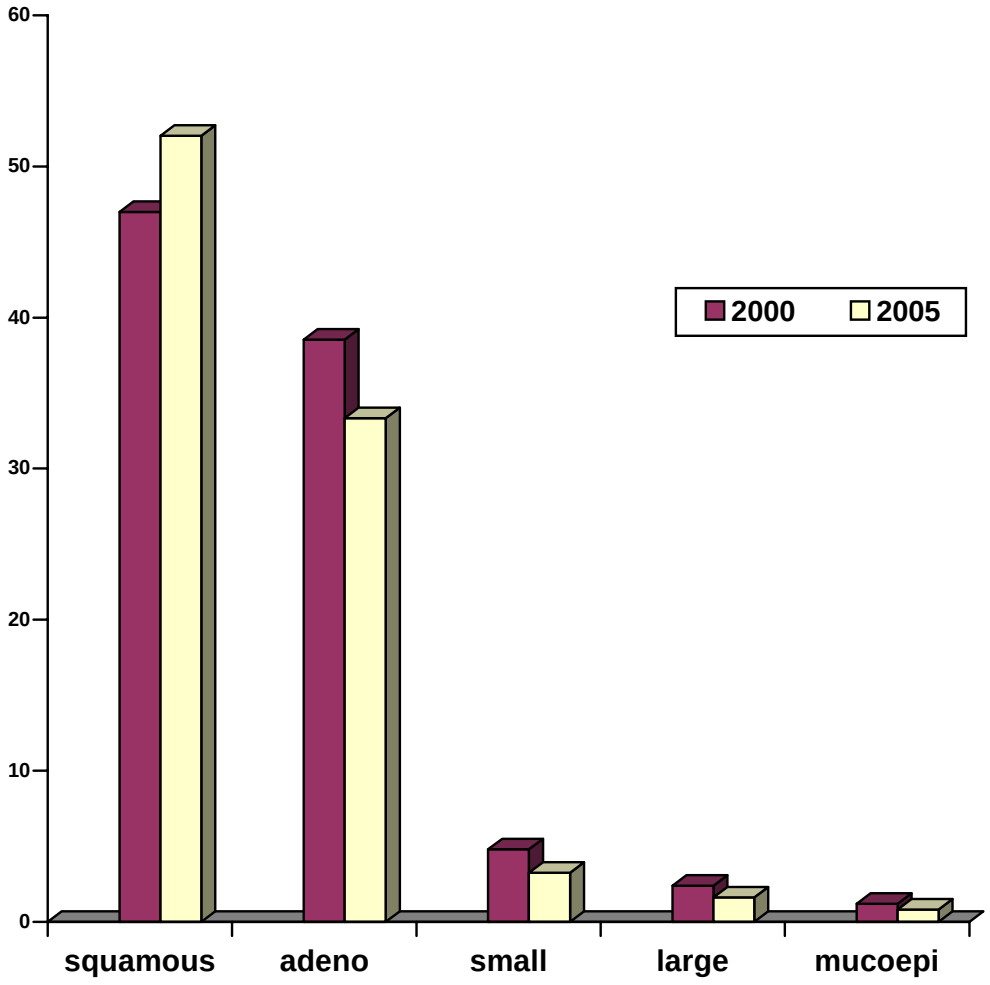
## SPECIFIC HISTOLOGICAL TYPES IN THIS STUDY

| Histological types | No. of patients | Percentage |
|---|---|---|
| Sqamous cell carcinoma | 64 | 52.03 |
| Adeno carcinoma | 41 | 33.33 |
| Small cell carcinoma | 4 | 3.25 |
| Large cell carcinoma | 2 | 1.62 |
| Mucoepidermoid | 1 | 0.81 |
| Not typed | 11 | 8.94 |
| Total | 123 | 100.00 |

# SPECIFIC HISTOLOGICAL TYPES IN THIS STUDY



## COMPARITION OF CELL TYPES PAST AND PRESENT




***2000 study conducted by Institute of thoracic medicine - Chetpet**

# DISCUSSION

Lung cancer is becoming the most common cause of cancer death for both men and women and it is a growing world wide problem, especially, in developing countries like India. In the recent past there has been many advances in the early detection, staging, prevention and treatment of lung cancer. The histopathologic appearance of lung carcinoma remains an important guide to prognosis and treatment.

In this prospective study of 123 patients, 123 patients had confirmed pathological diagnosis but 11 patients had evidence of malignant cell but repeated sampling did not yield the cell type.

The mean age range was from 28 to 82 years. The maximum number of patients in this study was between 50-69 years. This is in corroboration with the studies conducted in India and abroad.

107 patients were males and 16 patients were females. The male: female ratio was 6.6:1. In a study conducted in Mumbai in 1999 the ratio was 4.2:1. The picture is not the same in certain countries and in Japan the studies have shown 3:8:1 ratio and raising numbers in female.

The most common Histopathological type among males was squamous cell carcinoma and the most common type among female was adenocarcinoma. This is in corroboration with other studies conducted in India.

The most common pulmonary symptom in this study was cough 103 patients followed by dyspnea 71 patients and chest pain 65 patients and hemoptysis 39 patients. The pulmonary symptoms were more common with squamous cell carcinoma. This is consistent with the study conducted in India in 1999 by PN Chhajed et al., at Mumbai.

24 patients of 123 patients gave history suggestive of tuberculosis and treatment for the same. The most common cell type among these patients was adeno carcinoma. This is in corroboration with the study conducted in India and abroad.

Smoking had been established beyond doubt as one of the definite risk factors foe Bronchogenic carcinoma. In this study 97 patients were smokers, 26 patients were non smokers. None of the female in this study was smokers. The most common cell type among smokers was squamous cell carcinoma followed by Adenocarcinoma. All 4 patients who had small cell carcinoma were smokers. All the patients who had large cell

and anaplastic carcinoma were smokers. Smoking index >300 showed a significant increase in the incidence of squamous cell carcinoma over other cell types. This is consistent with the studies conducted by PN Chhajed et al at Mumbai in 1999 and also in studies conducted by Samet JM and published in chest 1993.

Among non smokers the most common pathological diagnosis was Adenocarcinoma. This is in corroboration with studies conducted in India by Arora VK et al in 1990 and in the west by Budix E.al in oct 1999.

Clubbing was seen in 41 patients (33.33%) in this study and the most common cell type associate was squamous cell carcinoma. This is inn corroboration with the studies conducted by Baughman RPet.al in 1998 published in journal of clinical and experimental Rheumatology.

Chest x-ray analysis revealed that the commonest presentation was mass lesion which was seen in 84 patients (75%). This is in corroboration with the studies conducted in India and in the west.

Sputum cytology was positive in only 6 patients (4.87%) and the most common tumour associated was squamous cell carcinoma. Post

bronchoscopic cytology wasd positive in 8 patients (6.5%) cytological techniques have not improved or modified in the recent years probably that is why positive yield was low. Biopsy have been improved by immunohistochemistry and mucin staining probably that is why yield is more.

Computerized tomography study was done in 98 patients. Computerized tomography guided needle biopsy of suspected mass lesion was done in 60 patients,positive results were obtained in 45(75%) patients.this is slightly less in shanker-s et al at PGIMER(july 1998)

Fiberoptic bronchope was done in 56 cases fiberoptic bronchopy helped in 11 patients by way of endobronchial biopsy. The positive yield was 73.33%.this is high compared to study conducted by Vattana Thum A et al at Bangkok in Thailand whose yield was only 50% with out transbronchial needle aspiration(August 1999)

34 patients under went for USG guided biopsy and 29 patients were diagnosed this is close to the results done by Knudsen DV et al. at Denmark(1996 may).in 3 patients it was done twiceto get a definite cell type.

Histopathological analysis revealed that the commonest cell type in this study was squamous cell carcinoma 64(52.03%) patients , followed by adenocarcinoma followed by41(33.33%), 4(3.25%) patients had small cell carcinoma.2(1.62%) patients had large cell carcinoma. 1 (.88%) had mucoepidermoid carcinoma.Squamous cell carcinoma still remained the leading cause of lung cancer in this study. Adenocarcinoma remains the second most common histological subtype of lung cancer in this study.A study conducted at Hyderabad by Thippanna et al, showed that the predominant cell type was squamous cell carcinoma.

A study conducted in Mumbai by P.N.Chajed et al., showed adeno carcinoma was the predominant cell type which did not correlate with this studying the studies in United states by Samet J M., and Beckett W S., on epidemiology of lung cancer had shown adeno carcinoma to be the commest.The reasons cited by them mainly were raise in female smokers and change in smoking pattern.

# CONCLUSIONS

1. The most common pathological cell type in this study was squamous cell carcinoma followed by adenocarcinoma.

2. Male sex, age >50 years, history of tobacco smoking were still a risk factor for Lung cancer.

3. Male, female ratio 6.6:1

4. Adenocarcinoma was found to be the commonest cell type of cancer among females and non smokers.

5. Clubbing was most commonly associated with squamous cell carcinoma.

6. most common radiological presentation was mass lesion.

7. Fiberoptic bronchoscope biopsy and brushing, computerized tomography/ ultra sonogram core needle biopsy were valuable tools to get at tissue diagnosis in 80% of patients.

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